A Single-Center Experience With the Ross Procedure Over 20 Years

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Background. The Ross procedure offers several potential advantages in a young patient population. The widespread use of the procedure is still limited due to the technical challenge. Pulmonary homograft stenosis and autograft dilatation remain a matter of concern. We present the long-term outcome in a single center with special emphasis on mortality and need for valvular reintervention.

Methods. All patients who received a Ross procedure as freestanding root replacement (modified Yacoub technique) at our institution between 1991 and 2011 were followed. Descriptive statistical methods and Kaplan-Meier analyses were performed.

Results. A total of 246 patients (191 males, 55 females) underwent the Ross procedure during the study period. There were 176 adults and 70 pediatric patients with an average age of 36 ± 10 and 10 ± 5 years, respectively. The median follow-up was 10 years. Twelve (4.9%) subjects were lost to follow-up. Early mortality was 1.6%. Overall mortality was comparable with an age and sex matched population for adult patients. The linearized risk for reoperation per patient-year was 0.6% for the autograft and 0.6% for the right ventricular outflow tract, with a mean time to surgery of 6.4 ± 4.9 years. Overall freedom from reintervention was 95% at 5 years, 88% at 10 years, and 81% at 15 years.

Conclusions. The Ross procedure provides good early results and an excellent long-term survival. It represents an excellent method of aortic valve replacement in children and young adults. Root reinforcement techniques and aortic reduction plasty may be beneficial, especially in adult patients with native aortic valve regurgitation.


The Ross procedure represents a valuable solution for young patients referred for aortic valve replacement [1]. It was first proposed by Donald Ross in 1962. The diseased aortic valve is replaced with the patient’s own pulmonary valve, the so-called pulmonary autograft. In addition, a pulmonary homograft is used for right ventricular outflow tract reconstruction. While it offers several advantages, it never gained widespread use due to its technical complexity and the fact that reinterventions on the autograft and homograft are required in a considerable number of patients [2–5].

Out of all valve replacement options, the pulmonary autograft comes closest to the native valve in hemodynamic profile with low transvalvular gradients, large effective orifice area, and laminar flow [6]. In comparison with prosthetic devices, especially mechanical valves, autografts exhibit a very low thrombogenicity and no necessity of anticoagulation. Further, the benefits of autologous tissue are a lower risk of infection and a reduced rate of degeneration. Of particular importance for the pediatric patient population is the ability of the autograft to grow [7–11]. Alternative approaches for young patients are mechanical valve replacement or aortic homograft implantation, but survival is worse and valve-related complications and bleeding might significantly impair quality of life and increase morbidity, and also mortality after valve replacement [12–15].

Despite all the benefits and advantages described above, the Ross procedure remains controversial. The aim of the current study is to evaluate this highly demanding surgical procedure 20 years after introduction at our center. Special emphasis is placed on survival and reoperations in the adult and pediatric Ross population.
Patients and Methods

Patients
All patients who underwent a Ross procedure with intra-annular implantation of the autograft as a freestanding root (modified Yacoub technique) at the Medical University of Vienna and Vienna General Hospital between 1991 and 2011 were included in this analysis. The Ross procedure was offered to eligible patients younger than 40 years by those surgeons at our institution who favored this operation. Furthermore, it was performed in older patients at their own request if considered as appropriate. Since 1991, it has been performed in 34% of non-elderly patients. Alternative surgical strategies comprised of mechanical valve replacement (40%), biologic valve replacement (15%), and aortic root replacement with a homograft (11%). The first 4 patients at our institution had a supra-annular implantation technique and were therefore not included in the analysis. Patients were divided according to their age in an adult (18 to 59 years of age) and a pediatric (<18 years) group. Preoperative data, procedure-related information, and the early postoperative course were collected in the Ross database and completed with follow-up visits when available and data from the hospital information system. For long-term follow-up, patients were contacted through telephone, a follow-up of the clinical history was performed, and all patients were instructed to perform an annual follow-up including clinical examination, medical history, and echocardiography. Seventy-two percent of all patients had their last follow-up between 2009 and 2011. Furthermore, mortality was cross-checked with the Austrian Federal Statistical Agency, providing a complete mortality follow-up until December 31, 2011. Our local Ethics Committee approved this study.

Surgical Technique
We performed a modified Yacoub technique for intra-annular autograft implantation as described previously [6, 16]. The inverted autograft was anastomosed with a 4-0 polypropylene running suture. The suture line was made slightly below the annulus through the subcommissural trigone for intra-annular implantation (Fig 1A). In cases of annular dilatation or mismatch to a smaller autograft, the annulus was reduced using a plication stitch (braided 2-0) at the most dilated commissure. If necessary, 1 or more stitches at other subcommissural triangles were placed to achieve a tight fit. For bicuspid valves, the autograft was inserted deep in the subcommissural area of the left-noncoronary commissure. The left facing sinus of the pulmonary valve was implanted as the new left coronary sinus. The length of the autograft root was kept as short as possible in order to avoid the potential for root dilatation. This resulted in a distal anastomosis 2 to 3 mm above the sinotubular junction. If size discrepancies were present, the aorta was always

Fig 1. Technical specifications of the Ross procedure. (A) Intra-annular implantation of the autograft; (B) aortic reduction plasty; (C) wrapping of the autograft with the remnant aortic wall; (D) wrapping of the autograft with a vicryl mesh.
Table 1. Procedural Specifications

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 246)</th>
<th>Pediatric (n = 70)</th>
<th>Adult (n = 176)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ross-Konno</td>
<td>4 (2%)</td>
<td>4 (6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Annular reduction</td>
<td>53 (22%)</td>
<td>13 (19%)</td>
<td>40 (24%)</td>
</tr>
<tr>
<td>Annular enlargement</td>
<td>7 (3%)</td>
<td>6 (9%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Concomitant procedures</td>
<td>34 (14%)</td>
<td>16 (23%)</td>
<td>18 (10%)</td>
</tr>
<tr>
<td>Reduction of the ascending aorta</td>
<td>70 (29%)</td>
<td>17 (24%)</td>
<td>53 (30%)</td>
</tr>
<tr>
<td>Vincryl mesh wrapping</td>
<td>47 (19%)</td>
<td>11 (16%)</td>
<td>36 (21%)</td>
</tr>
<tr>
<td>Aortic wrapping</td>
<td>49 (20%)</td>
<td>10 (14%)</td>
<td>39 (22%)</td>
</tr>
<tr>
<td>ECC (minutes)</td>
<td>185 ± 30</td>
<td>181 ± 36</td>
<td>186 ± 29</td>
</tr>
<tr>
<td>ACT (minutes)</td>
<td>135 ± 28</td>
<td>127 ± 31</td>
<td>138 ± 27</td>
</tr>
<tr>
<td>Re-exploration for bleeding</td>
<td>8 (4%)</td>
<td>4 (7%)</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Revision coronary artery lesion</td>
<td>3 (1%)</td>
<td>1 (1%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Permanent pacemaker</td>
<td>3 (1%)</td>
<td>2 (3%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

ACT = aortic cross-clamp time; ECC = extracorporeal circulation.

adjusted to the pulmonary root and downsized as appropriate (Fig 1B). One surgeon created an additional support for the aortic root. Therefore, 47 patients received root reinforcement with a Vincryl mesh (Ethicon, Inc, Somerville, NJ). An aortic wrapping using the residual aorta to support the pulmonary autograft was performed in 49 patients (Table 1; Figs 1C, 1D). Further procedural specifications are presented in Table 1. The pediatric population required more concomitant procedures (23% vs 10%; p = 0.01) and more annular enlargements (9% vs 1%, p = 0.004).

A pulmonary homograft was used in 238 patients. Homografts were either retrieved from the Vienna homograft bank or bought from CryoLife (CryoLife Inc, Kennesaw, GA). Xenografts were implanted in 8 patients. Two patients received a porcine Synergraft (CryoLife Inc), 2 patients received an Edwards Prima Plus stentless porcine bioprosthesis (Edwards Lifesciences LLC, Irvine, CA), 2 patients received a Polystan conduit (Polystan, Vaerlose, Denmark), and 2 patients received a Contegra pulmonary valved conduit (Medtronic Inc, Minneapolis, MN). All echocardiography studies were performed by trained cardiologists and pediatric cardiologists, or certified members of the Department of Cardiac Surgery.

Statistical Analyses

Statistical analyses were conducted according to the guidelines for reporting mortality and morbidity after cardiac valve interventions [17]. Hypothetical cumulative survival of an age-sex-matched standard population was computed by the life table method, based on age-sex-specific mortality data of the year 2000 published online by the Austrian Federal Statistical Agency (“Statistics Austria”). Cumulative survival and 95% confidence intervals for the study population were computed using the product-limit (Kaplan-Meier) method. Comparisons of survival of the Ross patients to that of the standard population at prespecified time points (5, 10, 15 years) were done using z tests based on the survival estimate and standard error, taking the standard population survival probability as null hypothesis value. A rather conservative approach for mortality evaluation was performed. Survival time was calculated until the last confirmed living follow-up, but all mortalities were additionally imported from the Austrian Federal Statistical Agency until the end of 2011. Therefore, actual survival may be better than reported. Reinterventions were defined as reoperations and catheter-based valve procedures on the autograft or the right ventricular outflow tract. For comparison of continuous data, t tests were performed. The χ² test was applied to compare categoric variables between groups. Linearized event rate per patient-year was calculated and compared between groups using the log-rank test. The 2-sided significance level was set to 5%. The R package (R Foundation for Statistical Computing, Vienna, Austria) and IBM PASW Statistics 18.0.3 (IBM, Armonk, NY) were used for statistical analysis.

Results

A total of 246 patients underwent a Ross procedure during the study period. Aortic regurgitation was the most frequent indication for surgery (40%). Combined aortic lesions and aortic stenosis were less frequent (31% and 29%, respectively). Perioperative data are presented in Table 1, patient characteristics are depicted in Table 2, and preoperative aortic valve patterns are shown in Table 3. The mean and median follow-up durations were 9 ± 5 and 10 (4; 12) years, respectively. Twelve (4.9%) subjects were lost to follow-up after hospital discharge. The majority of these patients were foreign citizens only transferred to our center for surgery. Therefore, these patients could not be followed and were excluded from any further analysis except operative outcome.

Mortality

Early mortality at 30 days was 1.6%. Reasons for death were acute myocardial dysfunction (2), bleeding complication associated with preexistent liver cirrhosis (1), and severe concomitant pathologies (1, several inborn malformations combined with a bleeding disorder). The valve-related mortality was 2.4% (0.3% per patient-year) and consisted of 1 porcine Synergraft failure and 1
ventricular fibrillation in the first postoperative year, 2 cases of septic endocarditis in intravenous drug-addicted patients, and 2 unknown causes of death.

An overall mortality of 5.7% was observed (0.7% per patient-year). In addition to the early and the valve-related mortality, 2 adult patients died (1 suicide and 1 liver cirrhosis) and 2 pediatric patients died (both in car accidents). The cumulative overall survival was compared with the age and sex matched Austrian overall survival data (Figs 2A, 2B). Five- and ten-year survival was statistically decreased in the complete Ross population (96% vs 99%; \( p = 0.022 \) and 94% vs 98%; \( p = 0.036 \)). Fifteen-year survival was not significantly different (91% vs 96%; \( p = 0.176 \)). The comparison of the adult group with the standard population showed no significantly different survival at 5, 10, and 15 years (Fig 2A). The decreased survival in the pediatric group compared with a standard population was only of borderline significance at all time points (\( p = 0.06, 0.05, \) and 0.07 for 5, 10, and 15 years; Fig 2B).

Reoperation and Reintervention

Twenty-three subjects (1.2% per patient-year) were reoperated on the autograft (n = 11, 0.6% per patient-year), the ascending aorta (n = 2, 0.1% per patient-year), or the right ventricular outflow tract (n = 11, 0.6% per patient-year) with a mean time to surgery of 6.4 ± 4.9 years. Freedom from reoperation was 95% after 5 years, 89% after 10 years, and 86% after 15 years. Six further patients received a Melody transcatheter pulmonary valve (Medtronic Inc) due to homograft stenosis. Overall freedom from reintervention was 95% at 5 years, 88% at 10 years, and 81% at 15 years.

Autograft Reoperation

The underlying aortic lesion, disease etiology, or dilatation of the ascending aorta was a non predictor for autograft reoperation in the whole study population. For adult Ross patients, native aortic valve regurgitation was associated with a significantly increased reoperation rate on the autograft (1.2% per patient-year) compared with aortic stenosis (0%) or combined lesions (0.5% per patient-year), respectively (\( p = 0.046 \)). Further, adult patients who received a concomitant reduction of the ascending aorta had a trend toward a decreased risk of reoperation on the autograft (0% vs 0.9% per patient-year; \( p = 0.054 \)).

In the early period of our Ross program, root reinforcement with a Vicryl mesh wrapping and wrapping with the residual aorta was performed (Table 1). Vicryl wrapping protected from autograft reoperation (0% vs 0.8% per patient-year; \( p = 0.014 \)). In 6 autograft reoperations, structural valve disease was the indication for surgery. In 4 of these patients, a technical problem of the root replacement contributed to the reoperation (leaflet perforation, n = 2; and distortion of the root, n = 2). Two patients had structural valve disease due to leaflet degeneration. Reoperation due to nonstructural valve disease, all caused by autograft dilatation, was performed in 4 patients. One reoperation was done in a patient with treated endocarditis.

One autograft was reconstructed by use of the David procedure and 2 valves with leaflet perforation could be reconstructed with a pericardial patch. In seven patients, the autograft had to be replaced with a mechanical heart valve (3 Bentall procedures) and 1 patient received a biologic heart valve. In addition, 2 isolated replacements of the ascending aorta were performed without intervention on the autograft.

Right Ventricular Outflow Tract Reintervention

Eleven reoperations and 6 catheter-based valve implantations were performed on the right ventricular outflow tract, one of the reoperations in combination with an autograft procedure. Four of the reinterventions were done during active, or after treated, endocarditis; 3 of these patients were intravenous drug dependent. Seven replacements and 6 catheter-based procedures were necessary due to structural valve disease. Reoperations were significantly more frequent in xenografts than in homografts (25% vs 4%; \( p = 0.016 \)). The percentages of reoperations and overall reinterventions were significantly higher in the pediatric group (9% vs 3%; \( p = 0.05 \) and 16% vs 3%; \( p = 0.001 \)). One porcine Synchron graft was prophylactically changed as reported earlier and not calculated for time to reoperation [18].

Valve-Related Complications

One stroke with full recovery (0.05% per patient-year), 1 peripheral embolus (0.05% per patient-year) and 1 major

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### Table 2. Preoperative Patients Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 246)</th>
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<th>Adult (n = 176)</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>29 ± 15</td>
<td>10 ± 5</td>
<td>36 ± 10</td>
</tr>
<tr>
<td>Gender (male to female)</td>
<td>191:55</td>
<td>50:20</td>
<td>141:35</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>65 ± 21</td>
<td>40 ± 24</td>
<td>73 ± 13</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167 ± 19</td>
<td>145 ± 25</td>
<td>173 ± 11</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23 ± 4</td>
<td>20 ± 4</td>
<td>24 ± 3</td>
</tr>
<tr>
<td>Prior surgery</td>
<td>17%</td>
<td>37%</td>
<td>10%</td>
</tr>
<tr>
<td>Prior intervention</td>
<td>8%</td>
<td>26%</td>
<td>1%</td>
</tr>
</tbody>
</table>

### Table 3. Aortic Valve Diagnosis, Etiology, and Morphology

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 246)</th>
<th>Pediatric (n = 70)</th>
<th>Adult (n = 176)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital/bicuspid</td>
<td>74%</td>
<td>97%</td>
<td>64%</td>
</tr>
<tr>
<td>Endocarditis active</td>
<td>3%</td>
<td></td>
<td>4%</td>
</tr>
<tr>
<td>Endocarditis inactive</td>
<td>6%</td>
<td>1%</td>
<td>7%</td>
</tr>
<tr>
<td>Rheumatic</td>
<td>5%</td>
<td>1%</td>
<td>7%</td>
</tr>
<tr>
<td>Degenerative/unknown</td>
<td>11%</td>
<td></td>
<td>16%</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>29%</td>
<td>19%</td>
<td>34%</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>40%</td>
<td>36%</td>
<td>41%</td>
</tr>
<tr>
<td>Combined aortic lesion</td>
<td>31%</td>
<td>44%</td>
<td>25%</td>
</tr>
<tr>
<td>Aortic valve morphology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bicuspid</td>
<td>76%</td>
<td>80%</td>
<td>75%</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>24%</td>
<td>20%</td>
<td>26%</td>
</tr>
</tbody>
</table>
bleeding (0.05% per patient-year) in a patient with liver cirrhosis occurred. However, 9 patients suffered from endocarditis (0.45% per patient-year). Three of these patients were intravenous drug users and had therefore an increased risk of this complication.

Surgeons

A total number of 14 surgeons performed the Ross procedure over the last 20 years with a high variability in the number of procedures performed, ranging from 1 to 89 and in success rate. High volume surgeons with a total number of 40 or more procedures had a trend toward fewer reoperations and revisions for bleeding in the adult population (6% vs 12%; \( p = 0.14 \) and 1% vs 6%; \( p = 0.07 \)). The number of procedures done per year varied from 1 to 30.

At last follow-up, 83% were New York Heart Association (NYHA) class I, 14% NYHA class II, and 3% NYHA class III.

Comment

We report herein the results of 246 Ross procedures performed in 20 years at a single center. It should be emphasized that in this series of patients, aortic regurgitation due to root dilatation as well as bicuspid aortic valve were not a contraindication to the Ross operation. In fact, 40% of our population presented with aortic regurgitation and 29% required a reduction of the ascending aorta.

Our outcome regarding survival and reoperations is similar to prior reports and underline the value of this procedure [1, 6, 19]. While the survival is slightly reduced in comparison with the general population at 5 and 10 years, long-term follow-up reveals a survival comparable with the age and sex-matched general population at 15 years after surgery. Survival was comparable with the matched general population at 5, 10, and 15 years for adult patients. This emphasizes the major advantage over mechanical valve replacement, which is associated with a decreased survival [20]. However, a recent trial suggested comparable outcome regarding survival for mechanical aortic prosthesis, but had only 6 years mean follow-up and required a strict self-management anticoagulation therapy, which does not reflect general outpatient care [21]. The increased mortality in the pediatric group compared with the age- and sex-matched population is partly explained by the presence of concomitant complex heart disease.

Our data are based on a median follow-up of 10 years, which represents a long follow-up period compared with other recent series. A long follow-up is essential in the evaluation of the Ross procedure because autograft dilation and homograft dysfunction are time dependent processes.

Native aortic valve regurgitation represents a higher risk for autograft reoperation in the adult population as reported previously by other authors [19]. Patients with a bicuspid aortic valve had no increased risk for autograft reoperation. This is in the line with several recent reports, which identified native aortic valve regurgitation but not bicuspid aortic valve as a risk factor in Ross patients [1, 19]. We therefore cannot support the exclusion of patients with bicuspid aortic valves from the Ross operation.

Interestingly, concomitant reduction procedures of the ascending aorta in patients with a dilated aorta seemed to protect from autograft reoperation. The autograft implantation itself is demanding and should be performed with meticulous care. Four out of 11 autograft reoperations could be related at least to some degree to technical difficulties leading to aortic regurgitation. Wrapping of the autograft with a vicryl mesh protected from autograft reoperation. This is in the line with some previous publications, indicating the freestanding aortic root as a risk factor for reoperation [19, 22]. On the contrary, the free-standing root according to the Yacoub technique, also applied in our series, provides excellent long-term results [6, 23]. All Vicryl mesh-supported procedures in our cohort, which showed excellent results regarding reoperation, were performed by the same experienced surgeon, which also may reduce reoperation rate. We now consider supporting the autograft with a Valsalva prosthesis according to the technique described by Carrel in patients with pure aortic regurgitation with aortic aneurysm or significant dilation of the ascending aorta [24].

The conduit in the right ventricular outflow tract position was the second most likely indication for reoperation. Three subjects developed homograft endocarditis due to intravenous drug abuse. To our opinion, the Ross procedure should therefore be applied very restrictively in...
drug-addicted patients, as foreign material is implanted in the pulmonary circulation, which is prone to endocarditis after non-sterile injections.

Further, pediatric patients and xenograft implantation could be identified as risk factors for reoperation [25]. The pulmonary homograft is considered as the most reliable right ventricular outflow tract conduit. Early failure of the porcine Synergygraft accounted for 1 death and 1 reoperation [18]. Children had a significantly higher number of reoperations due to homograft failure, which is probably due to growth and early degeneration [25]. However, this procedure still represents the best option in pediatric patients with aortic valve disease [5]. The number of homograft reoperations might decrease due to further options provided by transcatheter pulmonary heart valves.

The observed early mortality of 1.6% is high for this young patient population. Therefore, certain rules should be followed to further improve outcome. Patients with anticipated complex surgical procedures due to additional cardiac pathologies including coronary artery disease, aneurysm of the ascending aorta extending to the aortic arch, as well as patients with other diseased valves should not undergo a Ross procedure. Surgical training and the impact of the learning curve are well known predictors of outcome in patients undergoing complex cardiac surgery procedures [26, 27]. The trend toward improved results in high volume surgeons suggests to limit this operation to certain surgeons and institutions.

Limitations
The analysis of periodic echocardiographic results was beyond the focus of the current trial. Therefore, valvular regurgitation and stenosis not requiring surgical intervention are not reported. Furthermore, the number of patients with a follow-up of greater than 15 years is low.

Conclusions
The Ross procedure employing a modified Yacoub technique provides good early results and an excellent long-term survival. It represents a valuable method of aortic valve replacement in children and young adults. Bicuspid aortic valves do not show a higher risk of reoperation, but native aortic regurgitation in the adult population is a risk factor for autograft reoperation. A liberal approach to concomitant reduction procedures of the ascending aorta is warranted. Root reinforcement techniques may be beneficial, especially in adult patients with native aortic valve regurgitation. Risk factors for right ventricular outflow tract reoperations are pediatric procedures, xenografts, and intravenous drug abuse. The very high technical level highlights the importance of surgical training and dedication to this procedure.

References


